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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/677,574	10/03/2000	Shuwei Yang	0942.4500004/RWE/BJD	1982

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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/677,574

Applicant(s)

YANG ET AL.

Examiner

Richard G Hutson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11, 12, 14, 15, 17, 18, 20, 37-40, 43, 44, 47, 48 and 50-82 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11, 12, 14, 15, 17, 18, 20, 37-40, 43, 44, 47, 48 and 50-82 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/29/2003 has been entered.

Applicants amendment of claims 1, 2, 5, 11, 12, 14, 15, 17, 18, 20, 37, 44, 47, 50, 55-61, 63, and the addition of claims 65-82, Paper of 10/29/2003, is acknowledged.

Claims 1-9, 11, 12, 14, 15, 17, 18, 20, 37-40, 43, 44, 47, 48 and 50-82 are still at issue and are present for examination.

Applicants' arguments filed on 10/29/2003, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection was stated in the previous office action as it applied to previous claim 5 and its recitation "... mutants, variants, fragments and derivatives thereof."

In response to this rejection applicants have amended claim 5, such that it is now drawn to "... mutants and fragments thereof."

Applicants continue to argue that the metes and bounds of mutants and fragments of said polymerases are clearly discernible to those skilled in the art in light of the functional and structural limitations of the polymerases set forth in claims 1 and 2, as well as the teachings at pages 21-25 and 36-53 of the specification. This argument is not found persuasive because while applicants argue that given the definiteness of such sequence homology comparisons (i.e. between polymerase X and polymerase Y), those skilled in the art would be apprised of the scope of the claims, applicants argument is unclear given that no such sequence limitations are included in the rejected claims.

The rejection remains for the reasons previously stated. As previously stated, expansion of this argument raises the issue that it is unclear which, if not all known DNA polymerases, would be considered a mutant of the polymerases listed in claim 5, such that claim 5 does not further limit claim 3.

The previous rejection of claims 5, 44, 50 and 63 as being indefinite in that each of these claims are drawn to the polymerase of claims 3, 43, 48 or 62, which are drawn to the DNA polymerase of claim 1 or 47, which is drawn to a nucleic acid polymerase that has been specifically modified at a position corresponding to Arg 722, Lys 726 or both Arg 722 and Lys 726 of a *Thermotoga neopolitana* polymerase is hereby withdrawn based on applicants amendment.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 11, 12, 14, 15, 17, 18, 20, 37-40, 43, 44, 45, 46, 47, 48, and 50-82, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office actions of 4/23/2002 and 4/29/2003 as it applied to the previous claims. In response to this rejection, applicants have amended the claims and added new claims and traverse this rejection as it applies to the new claims. Newly added claims 65-82 are included in the rejection for the reasons previously stated and repeated below for the previous claims.

The newly amended claims continue to be directed to all possible nucleic acid polymerases which have been modified or mutated at a position corresponding to Arg

722, Lys 726 or both Arg 722 and Lys 726 of a *Thermotoga neopolitana* polymerase and kits comprising said modified polymerases, with the additional proviso that under certain conditions the mutated amino acid not be a specified residue.

Applicants submit that relative to biotechnology inventions, the Federal Circuit has instructed that functional descriptions of biological material can satisfy the written description requirement if a structure / function correlation is known in the art. Applicants do not provide an adequate teaching of such a structure / function correlation for the claimed mutant polymerases and while the art does teach some structure/function correlations for certain classes or types of polymerases, such teachings do not adequately describe the claimed genus which is drawn to any such mutation of any polymerase. Applicants are further reminded that the currently rejected claims have minimal if any structural limitations.

Applicants continue to argue that the specification clearly discloses structural regions of the O-helix domains for different DNA and RNA polymerases at page 20 and that the specification clearly teaches and exemplifies how to generate mutations of polymerases for enhanced fidelity, reduced 3'-5' and/or 5'-3' exonuclease activities and/or reduced discriminatory activity against dideoxynucleotides. Thus applicants conclude that based on this disclosure and what was known in the art at the time of filing, applicants were in possession of what is now being claimed.

Applicants argument is not found persuasive because while applicants have disclosed the structural regions of the O-helix domain for a number of previously known DNA and RNA polymerases, and exemplified how to generate mutations of a Tne

polymerase for enhanced fidelity, reduced 3'-5' and/or 5'-3' exonuclease activities and/or reduced discriminatory activity against dideoxynucleotides, applicants have not adequately described the genus of polymerase mutants comprising **any** polymerase which has been modified at a position corresponding to Arg 722, Lys 726 or both Arg 722 and Lys 726 of a *Thermotoga neopolitana* polymerase, which includes polymerase variants of **any Pol I, Pol II or Pol III-type DNA polymerases as well as reverse transcriptases and telomerases, etc...**

Additionally, as previously stated, the skilled artisan may not be able to determine those amino acid residues which correspond to Arg 722 or Lys 726 for many of the modified polymerases of the claimed genus, much less be able to modify these amino acids such that the modification results in the desired activity.

While applicants argue that such an issue as above, is not relevant to compliance with the written description requirement, clearly if applicants are relying upon what is adequately described by the art, determination of the corresponding residues is relevant, because if those corresponding residues are unknown, how can the art or applicants adequately describe such mutant polymerases.

There is no disclosure of any particular structure to function/activity relationship for the claimed genus that of any mutant polymerase, as discussed above. Given the lack of species representative of the claimed genus, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-9, 11, 12, 14, 15, 17, 18, 20, 37-40, 43, 45, 46, 47-62, 64 and 65-82 are further rejected under this statute because the newly added limitation which recites "with the proviso that when said modification consists of a single amino acid substitution at either Arg722 or Lys 726, said substitution is an amino acid other than Ala, and with the proviso that when said modification consists of an amino acid substitution at Arg722, said substitution is an amino acid other than Pro, Trp, and Gln." (see claims 1 and 2) is not supported by the original specification and is thus considered new matter. Similarly the similar provisos of claims 14, 17, 47, 57, 59, are also rejected because they are not supported by the specification as originally filed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read 'R. G. Hutson', with a large, sweeping loop at the end.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rg
11/26/2003